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TOWNSEND and TOWNSEND and CREW LLP

By: Maisie C. Livengood

Attorney Docket No.: 019282-000110US

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## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

William J. Dower, et al.

Application No.: 09/661,927

Filed: September 14, 2000

For: SUBSTRATES AND SCREENING  
METHODS FOR TRANSPORT  
PROTEINS

Examiner: Epperson, Jon D.

Art Unit: 1639

RESPONSE TO SUPPLEMENTAL  
RESTRICTION REQUIREMENT

Assistant Commissioner for Patents  
Washington, D.C. 20231

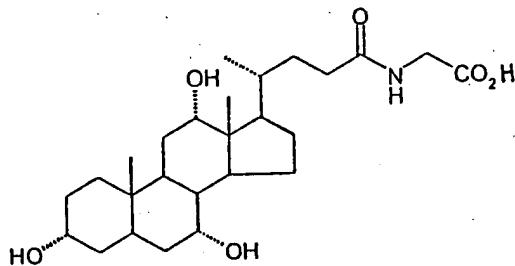
Sir:

This paper is filed in response to the Supplemental Restriction requirement mailed November 13, 2002, which has an initial deadline for response of December 13, 2002. A one month petition for an extension of time is enclosed, thus extending the period for response until January 13, 2003. Accordingly, this response is timely filed.

The Supplemental Restriction requirement requires that Applicants elect a single species of compound and a single species of complex. In both instances, specific chemical structures are required. With respect to the complex, the Office requires a specific structure for the compound, reporter and linker that make up the elected complex.

Compound

It is unclear to Applicants how they can elect a single species of compound since the method involves screening a *library* of complexes that have *different compounds*. Nonetheless, in the interest of furthering prosecution, Applicants elect a library that comprises a complex including glycocholic acid, the structure of which is shown below. Claims 1-63, 66 and 68 read on this species.

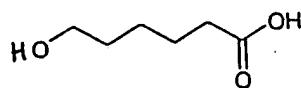


Complex

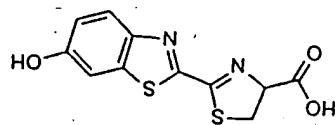
With regard to the complex, Applicants elect the following:

Compound: glycocholic acid shown above. Claims 1-63, 66 and 68 read on this species.

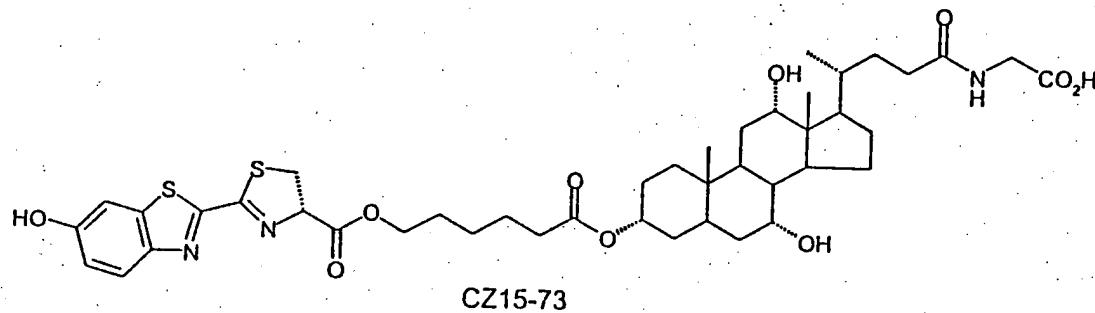
Linker: 6-hydroxy hexanoic acid (i.e., HOCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>COOH), the structure of which is shown below. Claims 1-54, 56, and 58-68 read on this species.



Reporter: Luciferin, the structure of which is shown below. Claims 1-3, 14-16, 18, 25, 36, 41-58, 64-68 read on this species.



A complex having these components is the molecule CZ15-73 shown in FIG. 17 and reproduced below. As required in the Supplemental Restriction Requirement, this molecule shows all the bonds of the elements that make up the complex.



Claims 1-3, 14-16, 18, 25, 36, 41-54, 56, 58, 66 and 68 read on this complex.

Detection of transport of this molecule into a cell is detected as described in claim 14. Specifically, the luciferin reporter serves as a substrate for luciferase enzyme expressed by the cell, which cell also expresses a carrier-type transport protein able to transport the molecule. Once transported into the cell, luciferase cleaves luciferin to generate a luminescent signal that can be detected by a luminescence detector (see, e.g., page 32, line 15 to page 33, line 24; and Example 7).

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Carrier-Type Transporter

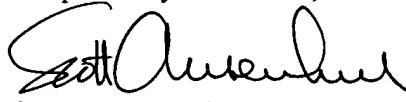
The Office further requires an election of species with respect to the type of carrier-type transport protein. In response, Applicants elect the ileal bile acid transporter (ASBT). Claims 1-68 read on this species.

Species of Detecting a Signal

Applicants wish to revise the election made in the prior response filed September 16, 2002, with respect to the type of signal detection. Instead of the signal detection approach described in claim 12, Applicants now elect the signal detection approach described in claim 14. In such methods, the reporter is a substrate for an enzyme. If the compound complexed with the reporter is a substrate for the carrier-type protein, the complex is transported by the carrier-type transport into a cell expressing the carrier-type transport protein and the enzyme. The enzyme then metabolizes the substrate to form a detectable product. Detection involves detecting the detectable product. Claims 1-3, 14-18, and 25-68 read on this species.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 303-571-4000.

Respectfully submitted,

  
Scott L. Ausenhus  
Reg. No. 42,271

TOWNSEND and TOWNSEND and CREW LLP  
Two Embarcadero Center, 8<sup>th</sup> Floor  
San Francisco, California 94111-3834  
Tel: 303-571-4000  
Fax: 415-576-0300  
SLA:sla  
DE 7091236 v1